

KIT gene

KIT proto-oncogene receptor tyrosine kinase

Normal Function

The *KIT* gene provides instructions for making a member of a protein family called receptor tyrosine kinases. Receptor tyrosine kinases transmit signals from the cell surface into the cell through a process called signal transduction. The KIT protein is found in the cell membrane of certain cell types where a specific protein, called stem cell factor, attaches (binds) to it. This binding turns on (activates) the KIT protein, which then activates other proteins inside the cell by adding a cluster of oxygen and phosphorus atoms (a phosphate group) at specific positions. This process, called phosphorylation, leads to the activation of a series of proteins in multiple signaling pathways.

The signaling pathways stimulated by the KIT protein control many important cellular processes such as cell growth and division (proliferation), survival, and movement (migration). KIT protein signaling is important for the development and function of certain cell types, including reproductive cells (germ cells), early blood cells (hematopoietic stem cells), white blood cells called mast cells, cells in the gastrointestinal tract called interstitial cells of Cajal (ICCs), and cells called melanocytes. Melanocytes produce the pigment melanin, which contributes to hair, eye, and skin color.

Health Conditions Related to Genetic Changes

Piebaldism

At least 69 *KIT* gene mutations have been identified in people with piebaldism. This condition is characterized by white patches of skin and hair caused by a lack of melanocytes in those areas. The mutations responsible for piebaldism lead to a nonfunctional KIT protein. The loss of KIT signaling is thought to disrupt melanocyte migration and proliferation during development, resulting in patches of skin that lack pigmentation.

Gastrointestinal stromal tumor

Mutations in the *KIT* gene are the most common genetic changes associated with gastrointestinal stromal tumors (GISTs). GISTs are a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine. In most cases,

these *KIT* gene mutations are acquired during a person's lifetime and are called somatic mutations. Somatic mutations, which lead to sporadic GISTs, are present only in the tumor cells and are not inherited. Less commonly, *KIT* gene mutations that increase the risk of developing GISTs are inherited from a parent, which can lead to familial GISTs.

KIT gene mutations associated with GISTs create a protein that no longer requires binding of the stem cell factor protein to be activated. As a result, the KIT protein and the signaling pathways are constantly turned on (constitutively activated), which increases the proliferation and survival of ICCs, leading to GIST formation.

Systemic mastocytosis

Somatic mutations in the *KIT* gene have been found to play a role in systemic mastocytosis. This condition is a blood disorder that typically appears after adolescence, varies in severity, and can affect many different body systems. Systemic mastocytosis occurs when mast cells abnormally accumulate in tissues. Mast cells normally trigger inflammation during an allergic reaction and signal an immune response when they are activated by an environmental trigger.

In most cases of systemic mastocytosis, the accumulated mast cells have a *KIT* gene mutation. More than 80 percent of individuals with systemic mastocytosis have a mutation in the *KIT* gene that replaces the protein building block (amino acid) aspartic acid with the amino acid valine at position 816 in the protein (Asp816Val or D816V). This and other *KIT* gene mutations result in production of altered proteins that are constitutively activated. As a result, signaling pathways that promote the proliferation of cells are overactive, which leads to increased production of mast cells and accumulation of the cells in various tissues. Cells with altered KIT proteins are more active than normal, leading to increased immune responses and signs and symptoms of systemic mastocytosis. In systemic mastocytosis, the excess mast cells lead to an increased immune response and signs and symptoms similar to an allergic reaction, such as skin redness and warmth (flushing), nausea, abdominal pain, nasal congestion, low blood pressure (hypotension), and headache.

Core binding factor acute myeloid leukemia

MedlinePlus Genetics provides information about Core binding factor acute myeloid leukemia

Other cancers

Somatic mutations in the *KIT* gene have been identified in several cancers. *KIT* gene mutations are involved in some cases of acute myeloid leukemia, which is a cancer of a type of blood cell known as myeloid cells, and sinonasal natural killer/T-cell lymphoma (NKTCL), another blood cell cancer that occurs in the nasal passages. In addition, some people with seminoma, a type of testicular cancer, have a somatic *KIT* gene mutation. The genetic changes involved in acute myeloid leukemia and seminomas lead to a KIT protein that is constitutively activated. The constant signaling causes overproliferation of the cells that make up these tumors. It is unclear how the *KIT* mutations in NKTCL are

involved in the condition.

Other Names for This Gene

- C-Kit
- CD117
- KIT_HUMAN
- mast/stem cell growth factor receptor Kit
- p145 c-kit
- PBT
- piebald trait protein
- proto-oncogene c-Kit
- proto-oncogene tyrosine-protein kinase Kit
- SCFR
- tyrosine-protein kinase Kit
- v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
- v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene-like protein

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of KIT ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3815\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3815[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28KIT%5BTI%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- KIT PROTOONCOGENE, RECEPTOR TYROSINE KINASE (<https://omim.org/entry/164920>)
- LEUKEMIA, ACUTE MYELOID (<https://omim.org/entry/601626>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/3815>)

- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=KIT\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=KIT[gene]))

References

- Dessinioti C, Stratigos AJ, Rigopoulos D, Katsambas AD. A review of genetic disorders of hypopigmentation: lessons learned from the biology of melanocytes. *Exp Dermatol*. 2009 Sep;18(9):741-9. doi: 10.1111/j.1600-0625.2009.00896.x. Epub 2009 Jun 23. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19555431>)
- Ezoe K, Holmes SA, Ho L, Bennett CP, Bologna JL, Brueton L, Burn J, Falabella R, Gatto EM, Ishii N, et al. Novel mutations and deletions of the KIT (steel factor receptor) gene in human piebaldism. *Am J Hum Genet*. 1995 Jan;56(1):58-66. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/7529964>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1801299/>)
- Falchi L, Verstovsek S. Kit Mutations: New Insights and Diagnostic Value. *Immunol Allergy Clin North Am*. 2018 Aug;38(3):411-428. doi:10.1016/j.iac.2018.04.005. Epub 2018 Jun 9. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/30007460>)
- Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, Kawano K, Hanada M, Kurata A, Takeda M, Muhammad Tunio G, Matsuzawa Y, Kanakura Y, Shinomura Y, Kitamura Y. Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. *Science*. 1998 Jan 23;279(5350):577-80. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9438854>)
- Hoermann G, Gleixner KV, Dinu GE, Kundi M, Greiner G, Wimazal F, Hadzijušević E, Mitterbauer G, Mannhalter C, Valent P, Sperr WR. The KIT D816V allele burden predicts survival in patients with mastocytosis and correlates with the WHO type of the disease. *Allergy*. 2014 Jun;69(6):810-3. doi:10.1111/all.12409. Epub 2014 Apr 17. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24750133>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4896381/>)
- Hongyo T, Li T, Syaifudin M, Baskar R, Ikeda H, Kanakura Y, Aozasa K, Nomura T. Specific c-kit mutations in sinonasal natural killer/T-cell lymphoma in China and Japan. *Cancer Res*. 2000 May 1;60(9):2345-7. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10811105>)
- Isozaki K, Terris B, Belghiti J, Schiffmann S, Hirota S, Vanderwinden JM. Germline-activating mutation in the kinase domain of KIT gene in familial gastrointestinal stromal tumors. *Am J Pathol*. 2000 Nov;157(5):1581-5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11073817>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1885736/>)
- Lim KH, Pardanani A, Tefferi A. KIT and mastocytosis. *Acta Haematol*. 2008;119(4):194-8. doi: 10.1159/000140630. Epub 2008 Jun 20. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18566536>)
- López V, Jordá E. Piebaldism in a 2-year-old girl. *Dermatol Online J*. 2011 Feb 15;17(2):13. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21382296>)
- Nakai Y, Nonomura N, Oka D, Shiba M, Arai Y, Nakayama M, Inoue H, Nishimura K,

Aozasa K, Mizutani Y, Miki T, Okuyama A. KIT (c-kit oncogene product) pathway is constitutively activated in human testicular germ cell tumors. *Biochem Biophys Res Commun*. 2005 Nov 11;337(1):289-96. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16188233>)

- Roskoski R Jr. Signaling by Kit protein-tyrosine kinase--the stem cell factor receptor. *Biochem Biophys Res Commun*. 2005 Nov 11;337(1):1-13. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16129412>)
- Spritz RA, Giebel LB, Holmes SA. Dominant negative and loss of function mutations of the c-kit (mast/stem cell growth factor receptor) proto-oncogene in human piebaldism. *Am J Hum Genet*. 1992 Feb;50(2):261-9. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/1370874>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1682440/>)
- Spritz RA. Molecular basis of human piebaldism. *J Invest Dermatol*. 1994 Nov;103(5 Suppl):137S-140S. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/7525736>)
- Spritz RA. Piebaldism, Waardenburg syndrome, and related disorders of melanocyte development. *Semin Cutan Med Surg*. 1997 Mar;16(1):15-23. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9125761>)
- Thomas I, Kihiczak GG, Fox MD, Janniger CK, Schwartz RA. Piebaldism: an update. *Int J Dermatol*. 2004 Oct;43(10):716-9. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15485525>)
- Tremblay D, Carreau N, Kremyanskaya M, Mascarenhas J. Systemic Mastocytosis: Clinical Update and Future Directions. *Clin Lymphoma Myeloma Leuk*. 2015 Dec;15(12):728-38. doi: 10.1016/j.clml.2015.07.644. Epub 2015 Aug 5. Review. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26382091>)

Genomic Location

The *KIT* gene is found on chromosome 4 (<https://medlineplus.gov/genetics/chromosome/4/>).

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